

## Feature Story

### The Enigmatic Olfactory Tubercle: An Understudied Part of the Brain That May Hold the Key to the Powerful Nature of Smell

By Robin Latham

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Why is it that a whiff of chlorine makes your best friend from grade school happy, remembering lazy summer days by the pool? But for you, it just reminds you of that heartbreaking summer when you were madly in love with a lifeguard.

It's well known that the same smell can be pleasant to one person, but unattractive to another. What makes an odor pleasing or offensive—what scientists call the hedonics of smell—is something that has puzzled researchers for decades. Yet no one has been able to locate where the association between smell and preference happens in the brain. But now, NIDCD researchers who study smell are beginning to take a fresh look at an understudied area of the brain that may play a key role in helping us decide why we turn our noses up at some smells and take another delightful sniff of others.

It might be hard to believe, but even today there are parts of the brain that aren't well explored. One such place is called the olfactory tubercle, an area located near the bottom of the front of the brain. The olfactory tubercle and the adjacent piriform cortex are major components of the olfactory system. They receive direct inputs from the olfactory bulb, which is connected to the specialized olfactory receptor neurons in the nose. Olfactory receptors are located in a small patch of tissue high inside the nose. They bind onto certain odor molecules and then transmit electrical signals to the olfactory bulb. The olfactory bulb sorts these signals and relays the message in the form of a smell-specific code to the olfactory tubercle and piriform cortex.

"It's a short, sweet system that allows for information to be extracted quickly," says Donald Wilson, Ph.D., an NIDCD-funded researcher at the New York University School of Medicine and the Nathan S. Kline Institute for Psychiatric



A whiff of chlorine can bring memories of a lazy summer by the pool.

Research in Orangeburg, N.Y. "In the olfactory system, you're only two synapses away from the important regions of the brain." In three steps, smell goes from an odor wafting outside the nose, to a signaled code, to a perception deep inside the brain. That means there aren't many places for olfactory code to be changed or attached to a certain preference.

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It might be hard to believe, but even today there are parts of the brain that aren't well explored. One such place is called the olfactory tubercle, an area located near the bottom of the front of the brain.

Surprisingly, even though the olfactory tubercle was identified more than a century ago as being part of the olfactory system, it is much better known for the role it plays in the brain's reward system. The tubercle is part of a pathway deep in the center of the brain, which includes a number of other structures, including the amygdala and the hippocampus (known for their role in learning, emotion, and memory). This pathway regulates and controls behavior through the release of dopamine, a neurotransmitter or chemical messenger in several reward and motivational systems of the brain.

"More than a thousand papers have been written in the last ten years about the link between the olfactory tubercle and the brain's reward system," says Wilson. "But from an olfactory point of view, we really don't know what happens in there once the signal arrives from the olfactory bulb."

A substantial amount of research had been done to map the olfactory tubercle's anatomy and neurochemistry in regard to olfaction, but functional studies had lagged behind. Wilson and one of his postdoctoral fellows, Daniel Wesson, Ph.D., decided to take a closer look. They were intrigued by the location of the olfactory tubercle at the nexus of the reward and olfactory systems and its potential for linking smell to preference. In spite of a lot of looking, no one had yet worked out where in the brain that link happened.

"If you look at the anatomy of the olfactory tubercle, it's in a prime position for performing this function," says Wesson. Information about smell streams into the piriform cortex and the olfactory tubercle, but only the tubercle is so intimately connected with the brain's reward system.

### What's Sound Got to Do with It?

The team set out to investigate the olfactory tubercle using mouse models. They planned their experiments around basic olfactory questions, such as whether the cells could discriminate between odors, which was something that had yet to be answered. But soon after they began, Wesson accidentally made a loud "clink" setting down his coffee mug next to the lab apparatus, and discovered that the tubercle cells responded to the sound. Sound? Wasn't it supposed to be smell?

Before they further explored the effect of sound, the team had to verify that the cells also responded to smell. They did. More than 65 percent of the tubercle cells were activated by at least one of the five odors presented. Some cells responded to single odorants and some responded to two or three or more. This was what the researchers had been hoping for—to show that the tubercle could discriminate among odors.

Then it got more interesting. The two decided to see if sound had any influence on the level of response to odor. They introduced different mixes of odors and tones to the cells and found that the response in almost a third of them was either elevated or suppressed depending on whether the tone was present with the odor. Sound was raising or lowering the response of the cells to smell.

Just what role sound might play in the whole process is unclear, but for Wesson and Wilson, this discovery has opened the door more widely to a new way of thinking about the role of the tubercle in the olfactory system. If sound can change the perception of odor in the tubercle, could there be other things going on in the tubercle that might influence our preferences for certain smells? Wilson is optimistic. "It could be that the olfactory tubercle is a multipurpose area and the olfactory information streaming in only connects with neurons that have nothing to do with reward, but that seems unlikely," says Wilson.

What seems more likely, and which will hopefully be revealed with further experiments, is that the olfactory tubercle, with its strong, direct input from the olfactory bulb and its direct links to arousal, reward, and emotional circuits, may be the place where associations between smell and pleasure or aversion happen. It could very well explain why smell is so tied up with our emotions that just a wisp of an odor can flood our minds with sweet memories or remind us of our first bout of unrequited love.

Read about Dr. Wesson's research in *The Journal of Neuroscience* at <http://www.jneurosci.org/cgi/content/full/30/8/3013>, or read the abstract in Pub Med at <http://www.pubmed.gov> and search for PMID 20181598.



## Recent Research and News

### 9/11 Workers Show Reduced Sensitivity to Odors, Irritants, Says New Research

Workers who breathed in a toxic mix of airborne chemicals, smoke, and dust in the wake of the September 11, 2001, World Trade Center disaster experienced a reduced ability to detect odors and irritants more than two years after they were exposed, says research published in the May 18 online issue of the journal *Environmental Health Perspectives*. The research, which was funded by the NIDCD, was conducted by scientists with the Monell Chemical Senses Center in Philadelphia, along with other collaborators.

"The nose performs many sensory functions that are critical for human health and safety," said lead author Pamela Dalton, Ph.D., in Monell's press release. "The sensory system that detects irritants

is the first line of defense to protect the lungs against airborne toxic chemicals. The loss of the ability of the nose to respond to a strong irritant means that the reflexes that protect the lungs from toxic exposures will not be triggered." According to other studies, thousands of individuals exposed to the World Trade Center site immediately following the disaster have developed chronic respiratory conditions.

The nose's ability to detect odors and irritants makes use of two highly sensitive and discriminating systems. Our sense of smell relies on olfactory receptors high in the nasal cavity that, upon attaching to specific odor molecules, will send signals to the brain, which are translated as a particular smell. Our chemical irritant

warning system relies on the trigeminal nerve, a nerve in the head that, when activated by a harmful chemical, causes your eyes to water and your nose to burn or sting. Under normal conditions, exposure to a chemical irritant will cause a person to reflexively sneeze and cough, protecting the lungs from damage. A person with reduced sensitivity, however, will be less likely to have this reaction.

Beginning in September 2003, the researchers examined 102 paid and volunteer World Trade Center responders who were on site at the time of and following the disaster and compared them to people of similar ages, genders, and job titles who weren't exposed. Ninety-seven percent of the World Trade Center group were near the lower Manhattan site during the week following the buildings' collapse, when the pollutants were likely at their highest. The researchers found that 22 percent of the workers were below the normal range in their ability to discriminate odors while nearly 75 percent showed a decreased ability to detect irritants. What's more, workers who were exposed to the dust cloud at the moment the buildings collapsed experienced the most damage in their ability to detect irritants, with individuals virtually unable to detect the test irritant n-butanol, a chemical that is used in the manufacture of many substances, including some drugs, plastics, and solvents.

The researchers next plan to screen a larger number of individuals who were exposed to the World Trade Center site in hopes of determining how extensive this health issue might be in 9/11 responders; they also plan to re-evaluate individuals who participated in the initial study to assess whether the problem persists, worsens, or recovers over time.

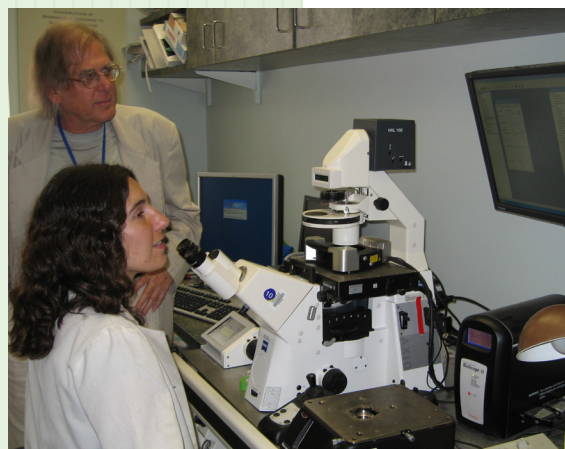
Read the article "Chemosensory Loss: Functional Consequences of the World Trade Center Disaster" in the journal *Environmental Health Perspectives* at <http://ehsehp03.niehs.nih.gov/article/citationList.action?articleURI=info%3Adoi%2F10.1289%2Fehp.1001924>, or read the abstract in Pub Med at <http://www.pubmed.gov> and search for PMID: 20478761.



Many 9-11 responders experienced a loss in their ability to detect odors and irritants.

## Good Vibrations: New Technique Uses High-Frequency Sound to More Realistically Measure Properties of Inner Ear

Biophysicists have a problem when they study the mechanical properties of tissues in the inner ear. The current technique, called atomic force microscopy (AFM), uses a microscopic probe on the end of a cantilever to apply force to a material and tell if it's stiff or soft, sometimes damaging the tissue in the process. In addition, measurements obtained with the standard AFM procedure don't provide a realistic picture for inner ear tissue



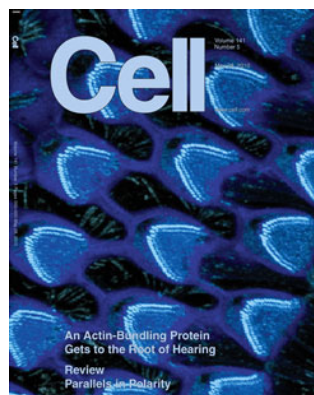
Drs. Chadwick and Gavara with their modified atomic force microscope, which uses high-frequency sound to determine properties of the inner ear.

since the tissue under the microscope isn't probed at the frequencies at which it typically functions. Drs. Richard Chadwick and Núria Gavara, of the NIDCD's Section on Auditory Mechanics, have implemented a new technique that allows them to study the mechanical properties of tissues at frequencies near the upper reaches of human hearing (about 20,000 hertz, or Hz), which has never been possible before, all while preserving the tissue. The

study is published in the journal *Nature Methods* at <http://www.nature.com/nmeth/journal/vaop/ncurrent/abs/nmeth.1474.html>. Read more on the NIDCD Web site at [http://www.nidcd.nih.gov/news/releases/10/06\\_20\\_10.htm](http://www.nidcd.nih.gov/news/releases/10/06_20_10.htm).

## A New Notion of How We Hear Takes Root

Although scientists are still working out the fine details of how we hear, they at least thought they had most of the major players nailed down. Now, new research published in the journal *Cell* shines a light on a cell structure in the inner ear that is more critical to hearing than anyone would have first guessed. An international research team led by NIDCD geneticist Thomas Friedman, Ph.D., has found that a structure at the base of a stereocilium (one of the bristly projections on



Rootlets (v-shaped light blue fluorescence) anchor stereocilia to the hair cell body, providing rigidity and durable flexibility to the hair bundle.

Credit: Cell

top of sensory hair cells in the inner ear) is also critical to the hearing process. The structure, called the rootlet, is a short connector piece between a stereocilium and a hair cell. "Obviously if you see something extending down into one structure, then up into another one, you think of it as an anchor. And it turns out that's true, but it does much more than that, and that actually surprised us," says Dr. Friedman. Read more in the journal *Cell* at <http://www.cell.com/abstract/S0092-8674%2810%2900368-5> or on the NIDCD Web site at [http://www.nidcd.nih.gov/news/releases/10/05\\_27\\_10.htm](http://www.nidcd.nih.gov/news/releases/10/05_27_10.htm).

## Traditional 'Heel Stick' Test Is Not an Effective Screening Tool for CMV in Newborns

A routine screening test for several metabolic and genetic disorders in newborns, the heel-stick procedure, is not effective in screening for cytomegalovirus (CMV) infection, a leading cause of hearing loss in children, according to research published in the *Journal of the American Medical Association*. The study, funded by the NIDCD, is part of a multicenter research project headed by the University of Alabama at Birmingham that is seeking to find the most effective screening test for CMV infection in newborns. The standard method for detecting CMV infection in newborns is labor-intensive and not conducive to a widespread screening program. Read more in the *Journal of the American Medical Association* at <http://jama.ama-assn.org/cgi/content/abstract/303/14/1375> or on the NIDCD Web site at [http://www.nidcd.nih.gov/news/releases/10/4\\_13\\_10.htm](http://www.nidcd.nih.gov/news/releases/10/4_13_10.htm).



## NIDCD Highlights

### Noisy Planet and Listen to Your Buds Take Hearing Protection Message to Schools

When it comes to protecting your hearing, it's never too early to start. That's why NIDCD's Noisy Planet campaign and the American Speech-Language-Hearing Association's (ASHA's) Listen to Your Buds campaign joined forces May 24-28 to bring the hearing protection message to elementary and middle schoolers throughout the D.C. Metro region. Staff from the two organizations pooled their time and resources to reach out to kids as young as pre-kindergartners all the way up to the Justin Bieber crowd.



For younger audiences, ASHA sponsored safe listening concerts in six elementary schools. Through the musical styles of children's GRAMMY award winners Cathy and Marcy, D.C. hip-hop artist Christylez Bacon, and songwriter and percussionist Billy Jonas, students were taught how

to listen to their personal music players safely, all while singing, dancing, clapping, and stomping to the beat. The concerts, which are held in collaboration with the Parents' Choice Foundation and the Consumer Electronics Association, were presented at the following schools: Sargent Shriver Elementary (Montgomery County, Md.), Patrick Henry Elementary (Arlington, Va.), Septima Clark Public Charter School (Washington, D.C.), Barnard Elementary (Washington, D.C.), Gaithersburg Elementary (Montgomery County, Md.), and Lyles Crouch Traditional Academy (Alexandria City, Va.).

For tween-aged audiences, NIDCD staff laced up their sneakers and loaded up their cars to deliver fun, science-based, hands-on presentations focusing on how loud noise affects hearing and how they can protect their hearing for life. In May, classrooms at Greenbelt and Samuel Ogle Middle Schools (Prince Georges County, Md.) took part in the activities, while Thurgood Marshall Middle School (Temple Hills, Md.) and Walker Mill

Middle School (Capitol Heights, Md.) received presentations in early June.

All told, more than 2,000 children received the hearing protection message over the week, which was offered as part of Better Hearing and Speech Month. A link to an article and a video of one of the concerts can be found on NIDCD's Noisy Planet Web site at [http://www.noisyplanet.nidcd.nih.gov/partner/np\\_message\\_to\\_schools](http://www.noisyplanet.nidcd.nih.gov/partner/np_message_to_schools).

**Noise in the News**  
Did you know that some World Cup soccer fans and players are worried about stadium noise levels? More information.

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All told, more than 2,000 children received the hearing protection message over the week, which was offered as part of Better Hearing and Speech Month. A link to an article and a video of one of the concerts can be found at the [USA/TV Channel 8](http://www.noisyplanet.nidcd.nih.gov/partner/) video site.

**Home**

**Noise and Hearing Loss**  
What everyone needs to hear

**For Parents**  
How to protect kids' hearing

**TweenZone**  
Facts and fun for 8- to 12-year-olds

**For the Community & Partners**  
What you can do to help

**For the Press**  
Information to share

**Order Materials**  
Order here

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News, research updates, and prevention tips for parents.  
Enter email address

### Would you like to schedule a presentation?

Teachers of students in grades 2-6 who are in the Washington, D.C., Metro region are welcome to schedule presentations for their classrooms, either for the summer or for next school-year. Likewise, parents of tweens in the Metro D.C. region are welcome to schedule a presentation for your parent-teacher organization or faith-based group. Please contact Robert Miranda-Acevedo at (301) 496-7243 or [miranda1@mail.nih.gov](mailto:miranda1@mail.nih.gov). To learn more about Noisy Planet partner activities, go to <http://www.noisyplanet.nidcd.nih.gov/partner/>.

## Robert J. Wenthold Memorial Lecture



Robert J. Wenthold, Ph.D.

On May 10, the NIDCD honored the memory of Robert Wenthold, Ph.D., who worked for the past two decades as a scientist, mentor, and administrator, and served as the NIDCD's scientific director from 1998 through 2008. The Robert J. Wenthold Memorial Lecture, titled *The Hair*

*Bundle's Protein Constellation*, by Peter Gillespie, Ph.D., of Oregon Health and Science University, was part of the NIH Neuroscience Seminar Series, and was held on the NIH Campus in Bethesda, Md. Dr. Gillespie's work is broadly focused on the mechanism of mechanotransduction by sensory hair cells of the inner ear.

Story Landis, Ph.D., Director of the National Institute of Neurological Disorders and Stroke welcomed participants to the lecture. The honor, she said, was earned after "arm wrestling" NIDCD Director James F. Battey, Jr., M.D., Ph.D. She shared an overview of Dr. Wenthold's scientific career, which focused on synaptic transmission and the biochemistry and localization of synaptic proteins. His landmark studies of the biochemistry of glutamate receptors are the foundation for the current understanding of these proteins. Glutamate is a chemical that stimulates neurons in the brain and is important in a host of functions including hearing, learning, and memory.

Dr. Battey made special acknowledgement of the Wenthold family, and presented Bob's wife Kris with a poster of the inaugural lecture. Among other family members present were their son Robert Jr., daughter Elisabeth Lucas, and granddaughter Marissa.

Watch the lecture on the NIH Web site at <http://videocast.nih.gov/Summary.asp?File=15880>.

## Summary of NIH Workshop on Non-Verbal School-Aged Children with Autism Available Online

In April 2010, the NIH convened a multidisciplinary workshop to discuss the state of the empirical knowledge about, and research opportunities regarding, the substantial subgroup of children with autism spectrum disorders (ASD) who have not developed functional verbal language by five years of age. Participants reviewed the current state of scientific knowledge, highlighted critical gaps in our knowledge, and identified research opportunities to address knowledge gaps. A series of presentations and group discussions addressed the three major topics of the workshop, including:

- Who are these children? What do we know about their developmental trajectories?
- How can we assess their skills and knowledge across different domains, with special reference to those abilities relevant to language acquisition?
- What treatments and interventions are effective in improving spoken language and communication in these children (augmentative and non-augmentative methods)?

View a more detailed description of the workshop on the NIDCD Web site at <http://www.nidcd.nih.gov/funding/programs/10autism>.



## Grants News

### NIDCD Grantee Elected to the National Academy of Sciences

King-Wai Yau, Ph.D., was recently elected to the National Academy of Sciences (NAS). Dr. Yau, an NIDCD grantee, is a well-respected scientist who studies both sight and smell, and has made major contributions to our understanding of the structure and function of biochemical elements in the sensing of visual stimuli in the retina. More recently, Dr. Yau expanded his innovative work to include mechanisms of sensory signaling in the olfactory system, advancing our understanding of how we sense odors through the study of a biochemical process, known as odor signal transduction, in which specific odors activate specific olfactory neurons. His concurrent studies in the detection of sensory stimuli in the eye and nose are revealing important similarities and differences between the two sensory systems.

Dr. Yau is a professor of neuroscience in the Solomon Snyder Department of Neuroscience at Johns Hopkins University School of Medicine, Baltimore. He received his Ph.D. in neurobiology



King-Wai Yau, Ph.D.

from Harvard University. In addition to his NIDCD funding, his research is supported by the National Eye Institute and the National Institute of Neurological Disorders and Stroke.

Dr. Yau is among 72 new American members recently elected to the NAS, which was created in 1863 by a congressional

charter approved by President Abraham Lincoln. The NAS is a private organization of scientists and engineers dedicated to furthering science and technology and using those advances for the general welfare. Election to the NAS is one of the highest honors to be bestowed upon a scientist or engineer.

## Meetings of Interest

### American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNSF)

September 26-29, Boston, Mass.

Web info: <http://am2010.entnet.org>



The Annual Meeting and OTO EXPO draws more than 9,000 medical experts and professionals

from around the world and this year will feature instruction courses, mini-seminars, scientific oral presentations, honorary guest lectures, and numerous scientific posters.

Visit the NIDCD booth (number 1342) in the exhibit hall at AAO-HNS.

### National Association of 4-H Extension Agents Annual Meeting

October 24-28, Phoenix, Ariz.

Web info: <http://www.2010nae4ha.org>



With the theme 4-H... *Your Passport to Success*, this year's annual meeting offers a varied program with seminars, speakers, and special events

for Extension 4-H Agents. Among the speakers are acclaimed teacher Rafe Esquith, author of *Teach Like Your Hair's on Fire*, and Dr. John Falk, expert on free choice learning, Department of Science and Mathematics Education, Oregon State University.



## American Public Health Association (APHA)

November 6-10, Denver, Colo.

**Web info:** <http://www.apha.org/meetings>



Learn from the experts in the field, hear about cutting-edge research and exceptional best practices, discover the latest public health products and

services, and share your public health experience with your peers. The world of public health is in continual motion, and there is no better way to stay abreast of the research and learn about emerging issues.

APHA's meeting program addresses current and emerging health science, policy, and practice issues in an effort to prevent disease and promote health.

## Society for Neuroscience (SfN)

November 13-17, San Diego, Calif.

**Web info:** <http://www.sfn.org/AM2010>

Through lectures, symposia, workshops, and events, the annual meeting is the premier venue for neuroscientists from around the world to debut cutting-edge research. Since 1971, the



meeting has offered attendees the opportunity to learn about the latest breakthroughs and network with colleagues throughout North America.

Visit the NIDCD booth (number 4112) in the exhibit hall at SfN.

## American Speech-Language-Hearing Association (ASHA)

November 18-20, Philadelphia, Pa.

**Web info:** <http://www.asha.org/events/convention>



*Leadership into New Frontiers* focuses on what speech-language-hearing professionals need to make a

difference in the lives of the people they serve. The convention will help each person discover her or his potential for leadership in everyday work and living. In addition to program sessions, a career fair, poster sessions, and other activities, the keynote speaker is Nancy Goodman Brinker, Founder of the Susan G. Komen Breast Cancer Foundation.

Visit the NIDCD booth (number 1132) in the exhibit hall at ASHA.

## Beyond NIDCD: News from Other Organizations

### National Cued Speech Association Offers Summer Cue Camps

The National Cued Speech Association sponsors several camps taking place this summer. Cue Camps provide a relaxing place to be with other cuers of all ages and stages. The next Cue Camps are:

#### Mackworth Island, Maine

July 28-August 1

Contact: Nicole Dobson at (207) 752-0417, or e-mail [ncldobson@yahoo.com](mailto:ncldobson@yahoo.com).

#### Jamestown, Va.

September 30-October 3

Contact: Maureen Bellamy at (703) 560-1035 or Rosemary Salvi at (703) 246-9892, or e-mail [NVCSA@yahoo.com](mailto:NVCSA@yahoo.com).





## Dangerous Decibels Educator Training Workshop

Learn to present a K-12 classroom program that is proven effective at changing knowledge, attitudes, and intended behaviors in students regarding their hearing health. This two-day workshop (16 hours) is led by hearing conservation, health communication, and educational outreach experts at Oregon Health and Science University, Portland State University, and the University of

Northern Colorado. The activities and lessons in the Dangerous Decibels classroom presentation are relevant for classes in biology, health, science, music, and shop.

The next Educator Training Workshop will be held August 12-13 in Portland, Oregon. For more information, contact Linda Howarth at (503) 494-0670, or e-mail [howarthl@ohsu.edu](mailto:howarthl@ohsu.edu). More information on Dangerous Decibels is available on the Web at <http://www.dangerousdecibels.org/>.

## New Resources

### NIDCD Web Site Gets New Look

NIDCD has launched its redesigned Web site, at <http://www.nidcd.nih.gov>. The updated site enhances accessibility and usability through several new features, including:

- A homepage slideshow to highlight new research developments and feature stories;
- Easier access to topics popular with a variety of audiences;
- Increased visibility for new funding opportunities.

updated examination-based estimates for sensory impairments in both categories overall and subgroups of older Americans.

Key findings include, among others:

- One out of four older Americans has impaired hearing; and three out of four have abnormal postural balance testing.
- Vision and hearing impairments each double in persons aged 80 years and over compared with persons aged 70-79 years.
- Balance problems are common among the poor.
- Of those with hearing problems, 72 percent might benefit from a hearing aid but do not use one.

Read or print the report on the Web at <http://www.cdc.gov/nchs/data/databriefs/db31.htm>.



The redesign updates the look and feel of the Web site, broadening its appeal to information seekers while retaining its in-depth, content-rich focus on the NIDCD's seven research areas of hearing, balance, smell, taste, voice, speech, and language.

Visit the redesigned site at <http://www.nidcd.nih.gov>.

## New Data on Sensory Impairments in Older Americans

The National Center on Health Statistics (NCHS), part of the Centers for Disease Control and Prevention, recently released the *NCHS Data Brief, Number 31*, "Vision, Hearing, Balance, and Sensory Impairment in Americans Age 70 and Over: United States, 1999-2006." The report provides

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**Voice: (800) 241-1044**  
**TTY: (800) 241-1055**  
**E-mail: [nidcdinfo@nidcd.nih.gov](mailto:nidcdinfo@nidcd.nih.gov)**